The work to be presented in the thesis entitled “Synthesis and studies of some heterocyclic compounds with biphenyl derivatives and their antimicrobial activities” has been divided into six chapters.

CHAPTER - 1: INTRODUCTION

Many important biochemical compounds and drugs of natural origin contain heterocyclic ring structures, which are found to be the key components in biological system. Significant numbers of compounds synthesized in the industrial sector each year are heterocyclic in nature. The presence of heterocyclic structure in such diverse type of compounds is strongly indicative of the profound effects. Such structures exert on physiological activity and recognition of this is abundantly reflected in efforts to useful synthetic drugs. Thus organic chemist need to be aware of the major new developments in this area. Some heterocyclic compounds must ideally have a broad spectrum of activity with a rapid bactericidal action. We must always continue to search

new heterocyclic molecules and identify its respective drugs activity. To take the care for synthesis new heterocyclic molecules a lower toxicity, a partial or total absence of undesirable side effects, more nutritive value, improved stability, a decrease in production cost and check the qualitative or quantitative improvement in activity with standard drugs.

Biphenyl methane and 4-aminopiperidine derivatives are highly versatile ring systems and well established medicinally useful class of compounds, because of their wide range of therapeutic and pharmacological properties like anti-microbial, anti-fungal, antihistaminic, analgesic, anti-tubercular, anthelmintic activity and antipsychotic agents[1-6]. Biphenyl derivative compound very useful in drugs. The discovery of the first potent and orally active nonpeptide AII antagonist, DuP 753 (losartan), has stimulated extensive research interest in this area, and numerous

derivatives have been reported as potent and selective antagonists[7]. Synthesized novel derivatives of imidazo[2,1-b][1,3,4]thiadiazole containing biphenyl moiety gives good to moderated antibacterial activity[8].

All the synthesized compounds were checked for the purity using TLC with mobile phase ethyl acetate and hexane for single spot. These were characterized by physical properties, elemental analysis, IR spectra and NMR spectra. Nuclear Magnetic Resonance (NMR) spectra of some selected compounds described in Chapter-2 to 6 has been studied out using TMS as internal standard in DMSO solvent.

CHAPTER - 2

Schiff bases represent one of the modest class of compounds possessing wide range of pharmacological activities like anticancer[9], antitumor[10], antibacterial[11] activity; they play a prominent part in the enzymatic or unenzymatic transaminating reactions of the carbonyl compounds with amino acids[12]. In the field of coordination chemistry very large number of schiff bases operates as ligands[13]. Some of the schiff bases are also used as insecticides, fungicides, herbicides[14],with the wide range of the biological action presented by the schiff bases derived from aromatic 2-hydroxyaldehydes[15].

Here in this chapter reaction of biphenyl-4-carboxylic acid hydrazide with different aldehydes in the presence of catalytic amount of acetic acid; gave biphenyl-4-carboxylic acid-(substituted benzylidene)-hydrazide.

CHAPTER - 3

As a part of surge of interest in heterocycles that have been explored for developing pharmaceutically important molecules, 4-thiazolidinones and 2-azetidinones have played an important role in medicinal chemistry.

2-Azetidinones have been extensively explored for their antibacterial[16], antitubecular[17], anticancer[18], and anti-inflammatory[19] activities. The thiazolidinones, substituted are reported to exhibit a wide variety of biological activity anthelmintics[20-21], cardiovascular[22], Mosquito repellant[23], antiviral[24], local anaesthetic[25]

This chapter represents the synthesis of biphenyl-4-carboxylic acid-([3-chloro-2-(substituted phenyl)-4-oxoazetidin-1-yl] amide and Biphenyl-4-carboxylic acid [2-(Substituted phenyl)-4-oxo-thiazolidin-3-yl]-amide that have been prepared by the condensation of biphenyl - 4 - carboxylic acid-(substituted benzylidene)-hydrazide with chloroacetyl chloride and mercaptoacetic acid respectively using catalyst.

CHAPTER - 4

Literature survey reveals that various imidazolinone derivatives possess a broad spectrum of activities which are reflected by their use as anticonvulsant[26] and anti-parkinsonian agents[27]. Some novel imidazolinones have been synthesized by using different oxazolones and condensing them with aliphatic and aromatic amines[28-29] and with sulphonamide as anticonvulsant agents[30].

Biphenyl-4-carboxylic acid [4-(substituted benzylidene)-5-oxo-2-phenyl-4, 5-dihydro-imidazol-1-yl]amide have been prepared by the condensation of 4-(substituted benzylidene)-2-phenyl-4H-oxazol-5-one and biphenyl-4-carboxylic acid hydrazide. 4-(substituted benzylidene)-2-phenyl-4H-oxazol-5-one derivatives, which were prepared by Erlenmeyer condensation of benzoyl glycine with different aldehydes in the presence of sodium acetate and acetic anhydride.

CHAPTER - 5

The benzylidene imidazolinone chemistry with its diverse biological properties like central nervous system depressant[31], anticonvulsant[32] and monoamineoxidaze inhibitor[33] has received importance in recent years.

In the present work biphenyl-4-carboxylic acid [4-{4-(substituted benzylidene)-5-oxo-2 phenyl-4,5-dihydro-imidazol-1-yl}-phenyl]-amide prepared by condensation between 3-(4-amino-phenyl)-5-(substituted benzylidene)-2-phenyl-3,5-dihydro-imidazol-4-one with biphenyl acid chloride, and 3-(4-amino-phenyl)-5-(substituted benzylidene)-2-phenyl-3,5-dihydro-imidazol-4-one have been prepared by condensation between 4-(substituted benzylidene)-2-phenyl-4H-oxazol-5-one and p-phenylene diamine.

CHAPTER - 6

The triazoles is well known moiety for a wide range of biological activity, several triazoles such as fluconazole, itraconazole are used as antifungal activity, the triazoles were also used antibacterial, anticonvulsant, antiplatelates, hypoglycemic agent[34-39].

5-Biphenyl-4-yl-4-[(substituted benzylidene)-amino]-4H-[1,2,4]triazole-3-thiol prepared by condensation between 4-amino-5-biphenyl-4-yl-4H-[1,2,4]triazole-3-thiol with substituted aldehyde, and 4-amino-5-biphenyl-4-yl-4H-[1,2,4]triazole-3-thiol prepared by condensation between Biphenyl-4-carboxylic acid hydrazide with carbon disulfide and then with hydrazine hydrate has been discussed in this chapter.

Infection is a major category of human disease and skilled management of antimicrobial drugs is of the first importance. The term chemotherapy is used for

the drug treatment of parasitic infections in which the parasites (viruses, bacteria, protozoa, fungi, and worms) are destroyed or removed without injuring the host.

The Danish physician Christian Gram in 1884 discovered a stain known as Gram stain, which can divide all bacteria into two classes "Gram positive" and "Gram negative". The Gram-positive bacteria resist decolouration with acetone, alcohol and remain stained (methyl violet) as dark blue colour, while Gram-negative bacteria are decolorized.

The biological screening of all the compounds prepared in (chapter 2 to 6) was carried out as mentioned below using agar diffusion method and results are described respectively. All the compounds were screened for their in vitro antimicrobial activity by measuring zone of inhibition in mm against different bacterial strains such as *Staphylococcus aureus* (gram positive), *Bacillus subtillis* (gram positive), *Escherichia coli* (gram negative) and *Klebsiella pneumonia* (gram negative) and fungi as *Candida albicans*. Standard drugs like Ampicillin and Flucanazole were used for the comparison. The antibacterial and anti fungal activities of all the synthesized compounds were screened and evaluated, the results are discussed in the chapters 2-6.

REFERENCES:

1. Dejaegher, Yves; Mangelinckx, Sven; Kimpe, Norbert De: S*ynlett* Issue 01, Pages 0113-0115, 2002.
2. John h. Billman, kwang m. Tai *J. Org. Chem.*, 23 (4), pp 535–539, 1958.
3. Mark A. Ashwell, William R. Solvibile Jr., Stella Han *Bioorganic & Medicinal Chemistry Letters*, Volume 11, Issue 24, Pages 3123-3127, 2001.
4. Ludovic Jean, Isabelle Baglin, Jacques Rouden, Jacques Maddaluno T*etrahedron Letters*, Volume 42, Issue 33, Pages 5645-5649, 2001.

5. Dina Manetti, Elisabetta Martini, Carla Ghelardini, *Bioorganic & Medicinal Chemistry Letters*, Volume 13, Issue 14, Pages 2303-2306, 2003.
6. Kristin M. Brinner, Mary Ann Powles, Dennis M. Schmatz *Bioorganic & Medicinal* Chemistry Letters, Volume 15, Issue 2, Pages 345-348, 2005.
7. Kurup, A.; Garg, R.; Carini, D. J.; Hansch, C. Chem. Rev.,101, 2727,2001.
8. Amandeep Kaur, Rajinder Kumar, Uday Kalidhar Research Journal of Pharmaceutical, Biological and Chemical Sciences ,Volume 3 Issue 2 Page No. 1096,2012
9. Schuster, I.S. and Robert, J.D., J. Org. Chem. 44, 2658, 1979.
10. Kong, D., Zhang, X., Zhu, Q., Xie, J. and Zhou, X. (1998) Zhongguo Yaown Huaxue Zazhi 8(4), 245; C.A., 131, 53640 p, 1999.
11. Rauhut, G., Clark, T. and Steinke, T, J. Amer. Chem. Soc. 115, 9174, 1993.
12. Scheehan, J. and Grenda, V.J., J. Amer. Chem. Soc. 84, 2417, 1962.
13. Pessoa, J.C., Cavaco, J., Covreia, J., Costa, D., Henriques, R.T. and Gillard, R.D., Inorg. Chim. Acta 305(1), 2000.
14. Alcock, N.W., Cook, D.F., McKenzie, E.D. and Worthington, J.M., Inorg. Chem. Acta 38, 107, 1980.
15. Popp, F.D., J. Org. Chem. 26, 1566, 1961.
16. Sharma P, Indapurkar P, Mandloi A, *Indian J Chem*, 37(B), 521, 1998.
17. Vashi B S, Mehta D S, Shah V H, *Indian J Chem*,34(B), 802, 1995.
18. Spletstoser J T, Flahertyh P T, Himes R H , Georg G I,*J Med. Chem*, 47, 6459, 2004.
19. Feigelson G B, Gurran W V, Ziegur C B, *US Appl*,672, 496c, 1991.
20. R. Govindon; *Fr. Demande,* 21, 08 834 (1972); *Chem. Abstr.*, 19, 32040k, 1973.
21. M. I. Husain & S. K. Agarwal; *Indian J. Pharm;* 37 89, 1975.
22. S. P. Singh, S. K. Anyoung & S. S. Parmar; *J. Pharm. Sci,* 63, 960, 1974.
23. W. A. Skinner, H. H. C. Tony, G. Bardy & T. E. Edward; *Chem. Abstr.*, 83, 189351t, 1975.
24. . T. Takematsu, K. Yokohama, K. Ideda, Y. Hayashi and E. Taniyamal; *Jpn. Patent,* 7 (51), 21 431 (1975); *Chem. Abstr.*, 84, 26880w, 1976.
25. A. K. El-Shafi, K. M. Hassan; *Curr. Sci.*, 52(13), 633-5 (1983); *Chem. Abstr.*, 100, 514974, 1984.

26. M. Verma, A.K. Chaturvedi, A. Chowdhari and S.S. Parmar. J. Pharm. Sci. 63, 1740, 1974.
27. P.K. Naithani, V.K. Srivastava, J.P. Barthwal, A.K. Saxena, T.K. Gupta and K. Shanker. Indian J. Chem. 28B, 990, 1989.
28. A.M.Dave, K.N.Bhatt, N.K.Undavia and P.B.Trivedi. J. Indian Chem. Soc. Vol. LXIV, 1987.
29. M.Z.Badr, A.H.El-Sherief and M.E.Tadros. J. Indian.Chem.Vol 20B, 1094-1094, 1981.
30. H. Joshi, P.Upadhyay, D.Karia and A.J.Baxi. Eur. J. Med. Chem. 38, 837-840, 2003.
31. TIWARI S S, AGARWAL R, SATSANGI R K. J. INDIAN CHEM. SOC., 57, 1040, 1970.
32. MUKHERJI D, NAUTIYI S R, PRASAD C R. INDIAN DRUGS. , 18, 125, 1981.
33. VERMA M, CHATRUVEDI A K, CHAUDHARI A, PARMAR S S., J. PHAM. SCI., 63, 1740, 1974.
34. Al-Deeb O.A – omar. EL – Brollosy N.R.Habib, T.M. El-emam A.A, "Arch Pharma (Weinheim), 339(1), 32-40, 2006.
35. B.Shivarama Holla, B.Veerendra, M.K Shivananda, N.Sucheta Kumari, "Indian journal of chemistry, 42B, 2010-2014, 2003.
36. Jag Mohan, "Indian journal of chemistry 42B, 401-404, 2003.
37. M.Y Mhasalkar, M.H.Shah, S.T. Nikam, K.G.Anantnarayanan, C.V. Deliwala,"Medicinal chemistry, 13(4), 4587-4593, 1970.
38. Krzysztof Sztanke, Kazimierz Pasternak, Anna Sidor-Wojtowiez, Janina Truchlinska and Krzysztof jozwiak, Bioogranic and Medicinal chemistry, 14(11), 3635-3636, 2006.
39. Yoshiko Kagoshima and Toshiyuki konosu," Journal of Flourine chemistry, 127(5), 643-650, 2006.

SIGNATURE OF SUPERVISING TEACHER

(Dr.G.M.Malik)
Department of Chemistry,
Navyug Science College, Surat.

SIGNATURE OF CANDIDATE

(Mr. A.V.PATEL)
Department of Chemistry,
Navyug Science College, Surat.